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EXAMINER	
SALMON, KATHERINE D	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,374	SU, XING	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,22-34,36-38 and 41-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17, 22-34, 36-38, 41-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to papers filed 2/26/2009.

2. Claims 1-17, 22-34, 36-38, 41-45 are pending. Claims 18-21, 35, and 39-40 have been cancelled.

3. The following rejections are newly applied as necessitated by amendment.

4. This action is FINAL.

Withdrawn Rejections

5. The rejection of the claims under 35 USC 112/2nd paragraph made in section 4 of the previous office action (11/25/2008) is moot based upon amendments to the claims.

6. The rejection of the claims under 35 USC 102 and 35 USC 103 made in section 5-12 of the previous office action (11/25/2008) is moot based upon amendments to the claims. Specifically it is acknowledged that although the art teaches a positively charged Raman signal enhancer, it does not teach a positively charged Raman signal enhancer maintaining a positive charge capable of interacting with a negatively charged species after binding. The 35 USC 103(a) rejections made below uses art of record in view of Ness et al. Ness et al. teaches tagging probes with a quaternary amine which is positively charge.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-2, 5-7, 9-10, 13-17, 33-34, 37-38, 42, 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US Patent Application Publication 2003/0211488 A1 November 13, 2003) in view of Ness et al. (US Patent 6027890 February 22, 2000).

With regard to Claim 1, Mirkin et al. teaches a multiplexed detection method of oligonucleotide targets bound to capture probes and detected using SERS (surface enhanced Raman) Raman probes (Abstract, p. 3 paragraphs 45-49). Mirkin et al. teaches contacting a target nucleic acid with a plurality of capture probes bound to a substrate forming a single-stranded overhang (Abstract, p. 3 paragraphs 45-49). Mirkin et al. teaches contacting the probe-target with a population of Raman-active oligonucleotides which forms a three-component sandwich assay used in a microarray (e.g. biochip) format composed of nanoparticle probes (Raman probes) detecting a bound target: capture probe duplex (Abstract, p. 3 paragraphs 45-49).
Mirkin et al. teaches a method in which the probe has a nanoparticle- Cy3-labeled alkylthiol capped oligonucleotide (Example 2, p. 10).

Further Mirkin et al. teaches that nanoparticles can be made of gold, silver or TiO2 (p. 7 paragraph 116) which are both positively charged. However, Mirkin et al.

does not teaches a positively charge Raman signal enhancer which maintains a positive charge capable of interacting with a negatively charged species.

With regard to Claim 2, Mirkin et al. teaches that the probe generates a Raman signal (paragraph 66 p. 5).

With regard to claim 5, Mirkin et al. teaches the positively charged Raman signal enhancer is a nanoparticle- Cy3-labeled alkylthiol capped oligonucleotide (Example 2, p. 10). This probe would be a composite of organic-inorganic nanoparticle (e.g. the oligonucleotide is organic and the Cy3 is inorganic).

With regard to Claims 6-7, Mirkin et al. teaches a method of detecting nucleotide occurrences at a target position wherein the position is a single nucleotide polymorphisms (abstract).

With regard to Claim 9, Mirkin et al. teaches a target segment which is equal to the combined nucleotides of the capture oligonucleotide probe and the Raman active oligonucleotide probe (Figure 4).

With regard to Claim 10, the claim is broadly interpreted to define the length of the Raman-active oligonucleotide probe as the entire length which would include the Cy3 and the nanoparticle attached to the end, Mirkin et al. teaches the probes include a A10 linker, which would make the probe longer than the target and therefore the target is less than the Raman active probe (Figure 4 and Example 4 paragraphs 162 p. 11).

With regard to Claim 13, Mirkin et al. teaches the target nucleic acid is isolated from a source and contacted to a population of capture oligonucleotide probes (Example 1 p. 10).

With regard to Claim 14, Mirkin et al. teaches a method wherein 500 pM of the nanoparticle probes are detected (e.g. less than a 1000 molecules) (p. 12 paragraph 167).

With regard to Claim 15, Mirkin et al teaches a method wherein the substrate is a biochip (p. 12 paragraph 167).

With regard to claim 16, Mirkin et al. teaches that the Raman active oligonucleotide probe is detected using SERS (abstract).

With regard to Claim 17, Mirkin et al teaches a method wherein a first population of Raman active oligonucleotide probes are contacted at a first spot and a second population of Raman active oligonucleotide probes are contacted at a second spot wherein the probe populations comprise at least one different oligonucleotide probe (Figure 7 and paragraph 14 p. 2).

With regard to Claim 37, Mirkin et al. teaches a portion of the overhang is a constituent of the target nucleic acid sequence (Figure 3A).

With regard to claim 38, Mirkin et al. teaches a nanoparticle- Cy3-labeled alkylthiol capped oligonucleotide (Example 2, p. 10). Therefore the probe comprises a tag (e.g. the alkylthiol cap).

With regard to Claims 41-42, Mirkin et al. teaches a method of aggregating nanoparticles with the Raman active probe and therefore aggregating the nanoparticles with the nucleic acid attached to the Raman signal enhancer (Figure 1).

With regard to Claim 44, Mirkin et al. teaches aggregation in the presence of a monovalent salt (p. 13 paragraph 174).

However, Mirkin et al. does not teaches a positively charge Raman single enhancer which maintains a positive charge capable of interacting with a negatively charged species.

Ness et al. teaches that the attachment of a positive charge amine to a nucleic acid as a tag allows for a positive charge under ionization conditions to give enhanced detectability (Column 16 lines 47-65). Ness et al. teaches one positive charge amine is a quaternary amine (Column 16 lines 47-65). The instant specification teaches a positively charged group attached to the Raman active oligonucleotide structure is a quaternary amino group (p. 7 paragraph 25). Therefore it is obvious the same structure (e.g. quaternary amine) would remain positively charged after binding to the probe.

With regard to Claims 33-34 and 43, Ness et al. teaches a quaternary amine structure which therefore would comprise a primary amine having an alkyl chain of 1 to 25 carbons.

With regard to Claim 45, Mirkin et al. and Ness et al. teaches a method wherein the nanoparticle can have a positive change using an amine charge (Column 16 lines 47-65). A heteroatom is any atom that is not carbon or hydrogen and therefore the teaching in Ness et al. teaches all the limitations of the claim.

Therefore it would be prima facie obvious to one of ordinary skill in the art at the time of filing the invention that the ordinary artisan would be motivated to modify the method of Mirkin et al. to replace the Cy3 label of the Raman active probe with the positively charged amine of Ness et al. The ordinary artisan would be motivated to modify the method of Mirkin et al. with positive charged amine tag of Ness et al.

because Ness et al. teaches that such a tag allows for a positive charge under ionization conditions to give enhanced detectability (Column 16 lines 47-65). Therefore using the amine tag of Ness et al. would enhance detectablity of the target.

8. Claim 3-4, 8, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US Patent Application Publication 2003/0211488 A1 November 13, 2003) in view of Ness et al. (US Patent 6027890 February 22, 2000) as applied to claims 1-2, 5-7, 9-10, 13-17, 33-34, 37-38, 42, 43-45 and further in view of Mirkin et al. (US Patent 6361944 March 26, 2002) (referred to as Mirkin B).

The teachings of Mirkin et al. and Ness et al. are previously discussed in this office action.

However, Mirkin et al. and Ness et al. do not teach Raman-active probes that comprise less than 5 or no purine residues.

Mirkin B teaches a method of detecting a nucleic acid using nanoparticles (Abstract). With regard to Claims 3-4, Mirkin B teaches a probe which comprises no purines (Seq Id No. 9 Figure 10).

With regard to Claim 8, Mirkin B teaches a method to detect multiple nucleotides mismatches in a target (e.g. a series of nucleotide occurrences at adjacent positions (Figure 12F).

With regard to claim 36, Mirkin B teaches a method to detect multiple nucleotides mismatches in a target (e.g. a series of nucleotide occurrences at adjacent positions (Figure 12F).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Mirkin et al. and Ness et al. to include the probe with no purines as taught by Mirkin B. The ordinary artisan would have been motivated to modify the method of Mirkin et al. and Ness et al. to include the probe with no purines as taught by Mirkin B because Mirkin B teaches that nanoparticles bearing only pyrimidine oligonucleotide bind in a sequence specific manner at purine and pyrimidine sites (Column 58 lines 15-25). Mirkin B. teaches that the binding allows for formation of triple-stranded complexes such that nanoparticle probes can be used for double stranded targets (Column 58 lines 15-25). Therefore the ordinary artisan would be motivated to use the probes of Mirkin B to detect double stranded targets.

9. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US Patent Application Publication 2003/0211488 A1 November 13, 2003) in view of Ness et al. (US Patent 6027890 February 22, 2000) as applied to claims 1-2, 5-7, 9-10, 13-17, 33-34, 37-38, 42, 43-45 and further in view of Pastinen et al. (Genome Research July 2000 Vol. 10(7) p. 1031).

The teachings of Mirkin et al. and Ness et al. are previously discussed in this office action.

However, Mirkin et al. and Ness et al. does not teach determining the entire target nucleic acid by aligning detected target sequences.

Pastinen et al. teaches a method of genotyping by allele-specific primer extension on a microarray (abstract).

With regard to Claim 11, Pastinen et al. teaches genotyping in which using primer extension a user can determine the sequence of the extended target (Abstract). Pastinen et al. teaches using a array of a multiplex of primers each specifically near a SNP area of detections (p. 1033 1st column last sentence and second column 1st paragraph). It is obvious to the ordinary artisan to use the teaching of Pastinen et al. aligning the nucleotides detected to determine which SNPs are present on both alleles.

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Mirkin et al. and Ness et al. to include the step of sequencing the target as taught by Pastinen et al. The ordinary artisan would have been motivated to modify the method of Mirkin et al. and Ness et al. to include the step of sequencing the target as taught by Pastinen et al. a method to perform high-throughput genotyping of samples in a parallel analysis method. The ordinary artisan would be motivated to use the method of Pastinen et al. to sequence the entire target in a quick assay to determine the entire sequence of the target.

10. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable Mirkin et al. (US Patent Application Publication 2003/0211488 A1 November 13, 2003) in view of Ness et al. (US Patent 6027890 February 22, 2000) as applied to claims 1-2, 5-7, 9-10, 13-17, 33-34, 37-38, 42, 43-45 and further in view of Lane et al. (US Patent 5,770,365

June 23, 1998).

The teachings of Mirkin et al. and Ness et al. are previously discussed in this office action.

However, Mirkin et al. and Ness et al. do not teach ligating the capture oligonucleotide probes to Raman-active oligonucleotide probes that bind to an adjacent segment of the target nucleic acid.

Lane et al. teaches a method of using nucleic acid capture moieties to detect nucleic acid sequences (Column 4, lines 19-25). Lane et al. teaches a labeled probe complementary to a target-complementary region of the capture moiety that is immobilized on insoluble support (Column 11, lines 30-35). With regard to Claim 12, Lane et al. teaches a method in which the detectable probe is ligated to the capture probe (a duplex-binding ligand binding site) (Figure 3).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Mirkin et al. and Ness et al to further include the use ligated probes as taught by Lane et al. The ordinary artisan would have been motivated to improve the method of Mirkin et al. and Ness et al. because Lane et al. teaches that the ligation method can be used for the detection of nucleic acid sequences, which do not occur near the terminus of an intact target strand (Column 12, lines 15-20).

11. Claims 22-24, 26-27, 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US Patent Application Publication 2003/0211488 A1

November 13, 2003) in view of Ness et al. (US Patent 6027890 February 22, 2000) and Chan et al. (US Patent Application Publication 2003/0059822 March 27, 2003) and Corbierre et al. (Journal of American Chem. Soc 2001 Vol. 123 p. 10411).

With regard to Claim 22, Mirkin et al. teaches a multiplexed detection method of oligonucleotide targets bound to capture probes and detected using SERS (surface enhanced Raman) Raman probes (Abstract, p. 3 paragraphs 45-49). Mirkin et al. teaches contacting a target nucleic acid with a plurality of capture probes bound to a substrate forming a single-stranded overhang (Abstract, p. 3 paragraphs 45-49). Mirkin et al. teaches contacting the probe-target with a population of Raman-active oligonucleotides which forms a three-component sandwich assay used in a microarray (e.g. biochip) format composed of nanoparticle probes (Raman probes) detecting a bound target: capture probe duplex (Abstract, p. 3 paragraphs 45-49).

Mirkin et al. teaches a multiplexed detection method of oligonucleotide targets bound to capture probes and detected using SERS (surface enhanced Raman) Raman probes (Abstract, p. 3 paragraphs 45-49). Mirkin et al. teaches contacting a target nucleic acid with a plurality of capture probes bound to a substrate forming a single-stranded overhang (Abstract, p. 3 paragraphs 45-49). Mirkin et al. teaches contacting the probe-target with a population of Raman-active oligonucleotides which forms a three-component sandwich assay used in a microarray (e.g. biochip) format composed of nanoparticle probes (Raman probes) detecting a bound target: capture probe duplex (Abstract, p. 3 paragraphs 45-49).

Further Mirkin et al. teaches that nanoparticles can be made of gold, silver or TiO2 (p. 7 paragraph 116) which are both positively charged. However, Mirkin et al. does not teaches a positively charge Raman single enhancer which maintains a positive charge capable of interacting with a negatively charged species.

With regard to Claim 23, Mirkin et al. teaches that a florescent signal is detected (Figure 8).

With regard to Claim 26, Mirkin et al. teaches that a Raman spectra is detected (abstract).

With regard to Claim 27, Mirkin et al. teaches comparing the signal to standard known Raman spectra labels (Figure 8). Therefore Cao et al. compares the detected spectra with known spectrum to identify the nucleotide occurrence.

However, Mirkin et al. does not teaches a positively charge Raman single enhancer which maintains a positive charge capable of interacting with a negatively charged species. However, Mirkin et al. do not teach a method of labeling the target with two labels, applying premade aggregates of metallic colloids to the probe-target, and applying an alternating current.

With regard to Claim 22, Ness et al. teaches that the attachment of a positive charge amine to a nucleic acid as a tag allows for a positive charge under ionization conditions to give enhanced detectability (Column 16 lines 47-65). Ness et al. teaches one positive charge amine is a quaternary amine (Column 16 lines 47-65). The instant specification teaches a positively charged group attached to the Taman active oligonucleotide structure is a quaternary amino group (p. 7 paragraph 25).

Chan et al. teaches a method for spatial resolution of signal detection (Abstract). With regard to Claim 22, Chan et al. teaches a method of passing a target through an optical detector to read florescent signals (p. 12 paragraphs 114 and 115). Chan et al. teaches the probe can be labeled with FRET labels (e.g. two labels on the probe) (paragraph 148 p. 16). Chan et al. teaches that the target nucleotide is pulled through the nanoslit of the channel by applying an alternating current (AC current) filed to the metal layer (p. 14 paragraph 132).

With regard to Claim 24, Chan et al. teaches the probe can be labeled with FRET labels (paragraph 148 p. 16).

With regard to Claim 29, Chan et al. teaches determining a series of nucleotide occurrences for one target by determination of a population of labeled probes (Figure 2 and paragraph 41 p. 4).

With regard to Claim 30, Chan et al. teaches passing the complexes through an optical detector to read the fluorescent signal (p. 12 paragraph 115).

With regard to Claim 31, Chan et al. teaches an interactor station comprised of the channel and the optical detector (e.g. a microelectromechical system) (p. 12 paragraph 115).

With regard to Claim 32, Chan et al. teaches that the target nucleotide is pulled through the nanoslit of the channel by applying an alternating current (AC current) filed to the metal layer (p. 14 paragraph 132). Chan et al. teaches the optical system uses radiation modulated frequencies (AC current oscillations) in the range of 10 MHz to 1 GHz (p. 15 paragraph 138).

With regard to Claim 22, Corbierre et al. teaches a method of synthesizing nanoparticles such as gold before incorporation (p. 10411 2nd paragraph). Corbierre et al. teaches a method of making pre-made nanoparticles (p. 10411 2nd paragraph).

Therefore it would be prima facie obvious to one of ordinary skill in the art at the time of filing the invention that the ordinary artisan would be motivated to modify the method of Mirkin et al. to replace the Cy3 label of the Raman active probe with the positively charged amine of Ness et al. and modify the method of Mirkin et al. to further include the use of a AC current and two label FRET system as taught by Chan et al. and premade gold nanoparticles as taught by Corbierre et al. The ordinary artisan would be motivated to modify the method of Mirkin et al. with positive charged amine tag of Ness et al. because Ness et al. teaches that such a tag allows for a positive charge under ionization conditions to give enhanced detectability (Column 16 lines 47-65). Therefore using the amine tag of Ness et al. would enhance detectability of the target. The ordinary artisan would have been motivated to modify the method of Mirkin et al. to further include the use of a AC current and two label FRET system as taught by Chan et al. because Chan et al. teaches a method of linear analysis of DNA which can allow for the development of specific sequences to be used in sequence-specific tagging and differentially tagging to increase resolution (p. 1 paragraph 3 and 4). The ordinary artisan would have been motivated to modify the method of Mirkin et al. to further include the use of a premade gold nanoparticles as taught by Corbierre et al., because Corbierre et al. teaches that premade nanoparticles provides full synthetic control over the making of the nanoparticle (p. 10412 last paragraph).

12. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US Patent Application Publication 2003/0211488 A1 November 13, 2003) in view of Ness et al. (US Patent 6027890 February 22, 2000), Chan et al. (US Patent Application Publication 2003/0059822 March 27, 2003) and Corbierre et al. (Journal of American Chem. Soc 2001 Vol. 123 p. 10411) as applied to claims 22-24, 26-27, and 29-32 above and further in view of Bruchez, Jr. et al. (US Patent Application 09/815585 March 21, 2002).

Neither Mirkin et al. or Ness et al. or Chan et al. or Corbierre et al. teach FRET labels of TAMRA and ROX.

With regard to Claim 25, Bruchez, Jr. et al. teach that the flurophores, which can be used as labels, include TAMRA and ROX (p. 13 paragraph 151).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Mirkin et al. , Chan et al., and Corbierre et al. to further include any type of FRET labels including TAMRA and ROX as presented by Bruchez Jr. et al. The use of FRET labels is well known in the art and the use of different types of FRET labels are interchangeable. Therefore the ordinary artisan would use any type of FRET label for the method of Mirkin et al., Chan et al., and Corbierre et al. including TAMRA and ROX to detect nucleotide occurrences on a target strand.

13. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US Patent Application Publication 2003/0211488 A1 November 13, 2003), Ness et al. (US Patent 6027890 February 22, 2000), Chan et al. (US Patent Application Publication 2003/0059822 March 27, 2003) and Corbierre et al. (Journal of American Chem. Soc 2001 Vol. 123 p. 10411) as applied to claims 22-24, 26-27, and 29-32 above and in view of Livak et al (US Patent 5723591 March 3, 1998).

Neither Mirkin et al. nor Ness et al. or Chan et al. or Corbierre et al. teach the two labels are located about 3-6 nm apart.

With regard to Claim 28, Livak et al. teaches that the quencher molecule and reporter should be between 6-16 nucleotides (Column 3, line 63). The distance between nucleotides is 0.23 nm, therefore the distance between a reporter and quencher can be between 1.38 to 3.68 nm apart (between 3-6 nm).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Mirkin et al., Chan et al., and Corbierre et al. to further include distance limitation as taught by Livak et al. The ordinary artisan would have been motivated to modify the method of Mirkin et al., Chan et al., and Corbierre et al. to further include distance limitation as taught by Livak et al. because Livak et al. teaches that there is a distance that must be maintained between the quencher and reporter in order for the quencher to be able to quench the reporter in the assay (Column 3, lines 60-65).

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-17, 22-34, 36-38, 41-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-4 of copending Application No. 11414611. Although the conflicting claims are not

identical, they are not patentably distinct from each other. Claims 1, 4, 33, and 43 of the pending application are drawn to a method comprising a light source, a nucleic acid comprising a positively charged enhancer which is an amine, and detection of the Raman signal, which are identical in steps to Claims 1-4 of application 11/414611.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to arguments

The reply requests the double patient rejections be held in abeyance until the indication of allowable subject matter. As such the double patenting rejections have been maintained.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday-Friday 8AM-530PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Katherine Salmon/
Examiner, Art Unit 1634

/Sarae Bausch/
Primary Examiner, Art Unit 1634